Fucoidan extracted from Cladosiphon okamuranus Tokida induces apoptosis of human T-cell leukemia virus type 1-infected T-cell lines and primary adult T-cell leukemia cells.


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Adult T-cell leukemia (ATL) is caused by human T-cell leukemia virus type 1 (HTLV-1) and remains incurable. The highest endemic area of HTLV-1 carriers in Japan is located in Okinawa, and novel treatments are urgently needed in this area. We extracted fucoidan, a sulfated polysaccharide, from the brown seaweed Cladosiphon okamuranus Tokida cultivated in Okinawa, Japan and examined its tumor-suppression activity against ATL. Fucoidan significantly inhibited the growth of peripheral blood mononuclear cells of ATL patients and HTLV-1-infected T-cell lines but not that of normal peripheral blood mononuclear cells. Fucoidan induced apoptosis of HTLV-1-infected T-cell lines mediated through downregulation of cellular inhibitor of apoptosis protein-2 and survivin and G1 phase accumulation through the downregulation of cyclin D2, c-myc, and hyperphosphorylated form of the retinoblastoma tumor suppressor protein. Further analysis showed that fucoidan inactivated NF-kappaB and activator protein-1 and inhibited NF-kappaB-inducible chemokine, C-C chemokine ligand 5 (regulated on activation, normal T expressed and secreted) production, and homotypic cell-cell adhesion of HTLV-1-infected T-cell lines. In vivo use of fucoidan resulted in partial inhibition of growth of tumors of an HTLV-1-infected T-cell line transplanted subcutaneously in severe combined immune deficient mice. Our results indicate that fucoidan is a potentially useful therapeutic agent for patients with ATL.